# Synthesis of 1-[(Triisopropylsilyl)ethynyl]- $1\lambda^3$ ,2-benziodoxol-3(1*H*)-one and Alkynylation of Indoles, Thiophenes, and Anilines

Jonathan P. Brand, Jérôme Waser\*

Laboratory of Catalysis and Organic Synthesis, Ecole Polytechnique Fédérale de Lausanne EPFL SB ISIC LCSO, BCH 4306, 1015 Lausanne, Switzerland Fax +41(21)69397 00; E-Mail: jerome.waser@epfl.ch *Received: 19.01.2012; Accepted after revision: 24.02.2012* 



**Abstract:** An efficient procedure was developed for the synthesis of 1-[(triisopropylsilyl)ethynyl]- $1\lambda^3$ ,2-benziodoxol-3(1*H*)-one on a 100-mmol (36-g) scale. The benziodoxolone can be used for the gold-catalyzed direct alkynylation of indole, 2-hexylthiophene, or *N*,*N*-dibenzylaniline on a 5- to 10-mmol scale.

Key words: alkynes, arenes, catalysis, heterocycles, iodine



Scheme 1 Synthesis of 1-[(triisopropylsilyl)ethynyl]- $1\lambda^3$ , 2-benziodoxol-3(1*H*)-one (2) and its use in the direct alkynylation of (hetero)arenes

In addition to their use in oxidation reactions, hypervalent iodine reagents have become increasingly important as reactants in C–C bond-formation processes.<sup>1</sup> Togni and coworkers<sup>2</sup> have demonstrated the use of the cyclic benziodoxol(on)e structure in the transfer of trifluoromethyl groups, whereas we have demonstrated the use of benziodoxolones in alkyne transfer.<sup>3</sup> Togni showed that benziodoxol(on)es **3** and **4** (Figure 1) can be used for transfer of a trifluoromethyl group to malonates, nitro esters, or arenes.<sup>2</sup> We demonstrated that benziodoxolones **5** and **2** are superior to classical alkynyliodoniums salts<sup>4</sup> as reagents for the ethynylation of  $\beta$ -keto esters,  $\beta$ -nitro esters,  $\beta$ -cyano esters,<sup>5</sup> as well as for the oxy- and aminoalkynylation of alkenes.<sup>6</sup>



Figure 1 Benziodoxoles for trifluoromethyl and alkyne group transfer reactions

SYNTHESIS 2012, 44, 1155–1158 Advanced online publication: 22.03.2012 DOI: 10.1055/s-0031-1290589; Art ID: SS-2012-C0065-ST © Georg Thieme Verlag Stuttgart · New York The discovery of the reactivity of 1-[(triisopropylsilyl)ethynyl]- $1\lambda^3$ ,2-benziodoxol-3(1H)-one **(2**; TIPS-EBX) has also made an impact in the growing field of direct alkynylation of heterocycles and aromatics.<sup>7,8</sup> Alkynyl aromatics are normally synthesized by means of the Sonogashira reaction.<sup>9</sup> An alternative strategy is based on the use of an electrophilic alkyne and a nonfunctionalized nucleophilic arene in the presence of a metal catalyst. Reagent 2 has been shown to have unique properties for the gold-catalyzed alkynylation of indoles, pyrroles, thiophenes, and anilines.8 Here, we report a practical procedure for its synthesis together with its use in the direct alkynylation of indole, 2-hexylthiophene, and N,N-dibenzylaniline (Scheme 1).

In 1996, Zhdankin and co-workers reported the first synthesis of TIPS-EBX (2) on a 1.5-mmol scale.<sup>10</sup> This reagent was not used in organic synthesis until our recent work. To synthesize TIPS-EBX (2) in larger quantities, we first investigated the scaling up of the originally published procedure. The quality of the 2-iodosylbenzoic acid (1) precursor was crucial for the efficiency and reproducibility of the reaction. The protocol of Kraszkiewicz and Skulski<sup>11</sup> for preparing the acid 1 gave the best results in this respect (Scheme 2). Air drying gave a better quality of reagent than did drying under high vacuum. This synthesis was scaled up to 0.3 mol. Because of the thermal instability of hypervalent iodine compounds, *the reaction must be carried out behind a safety shield*.



Scheme 2 Synthesis of 2-iodosylbenzoic acid (1)

The other precursor, the bis-silvlated alkyne **8**, was synthesized by using a reported procedure (Scheme 3).<sup>12</sup>

Scheme 3 Synthesis of trimethylsilyl(triisopropylsilyl)ethyne (8)

Zhdankin's procedure was then modified for scale up (Scheme 4). On the larger scale, removal of pyridine by treatment with acid and removal of 2-iodobenzoic acid (6) by treatment with base were essential for efficient and reproducible purification. A single recrystallization from acetonitrile gave highly pure crystals that did not show any sign of decomposition after several months at room temperature in air.<sup>13</sup> When the procedure was scaled up to 100 mmol, it gave 36 g of compound **2** (85% yield).



Scheme 4 Synthesis of TIPS-EBX (2) from 2-iodosylbenzoic acid (1)

We then used TIPS-EBX (2) in the direct alkynylation of indole (9) by following our previously reported procedure (Scheme 5).<sup>8a</sup> The process is highly C3-regioselective and can be carried out under air and without drying of the solvent. On a 10-mmol scale, the use of 1 mol% of gold(I) chloride gave product **10** in 82% yield (2.4 g) after 36 h. 2-Iodobenzoic acid (6) could be recovered in 73% yield by acidification of the aqueous layer and extraction with ethyl acetate. The recycled compound can be converted back into TIPS-EBX (**2**) in two steps.



Scheme 5 Gold-catalyzed direct alkynylation of indole (9)

The C2-selective direct alkynylation of 2-hexylthiophene (11) was scaled up to a 10-mmol scale by using 1 mol% of gold(I) chloride and 1.2 equivalents of trifluoroacetic

acid to give product **12** in 81% isolated yield (2.8 g) (Scheme 5);<sup>8c</sup> 97% of the 2-iodobenzoic acid (6) was recovered. Product **12** is useful as a building block for organic materials.



Scheme 6 Gold-catalyzed direct alkynylation of 2-hexylthiophene (11)

Finally, *N*,*N*-dibenzylaniline (**13**) was successfully *para*alkynylated on a 5 mmol scale in 79% yield (1.97 g) at room temperature (Scheme 7);<sup>8d</sup> 13% of the starting material **13** and 72% of 2-iodobenzoic acid (**6**) were recovered.



Scheme 7 Gold-catalyzed direct alkynylation of *N*,*N*-dibenzylaniline (13)

In conclusion, we have developed an improved synthesis of TIPS-EBX (2) on a 100-mmol scale. Both indole (9) and 2-hexylthiophene (11) were successfully alkynylated in the presence of 1 mol% of gold(I) chloride under mild conditions on a 10-mmol scale whereas N,N-dibenzylaniline (13) was alkynylated in the presence 5 mol% of gold(I) chloride on a 5-mmol scale. Further investigations on synthetic applications of TIPS-EBX (2) are currently underway in our laboratory.

All reactions were carried out in oven-dried glassware under N2, unless otherwise stated. AuCl was purchased from Aldrich or Alfa Aesar and kept in desiccator under anhydrous condition. The catalyst showed a decrease in reactivity on prolonged exposure to air (~1 month). All chemicals were purchased and used as received, unless stated otherwise. Solvents were evaporated under reduced pressure at 40 °C on a Büchi Rotavapor. Melting points were measured on a calibrated Büchi B-540 melting-point apparatus in open glass capillaries. <sup>1</sup>H NMR spectra were recorded on a Brucker DPX-400 400-MHz spectrometer in  $CDCl_3$  or  $DMSO-d_6$ . All signals are reported in ppm with the internal chloroform signal at 7.26 ppm or the internal DMSO signal at 2.50 ppm as standard. <sup>13</sup>C NMR spectra were recorded with <sup>1</sup>H-decoupling on a Brucker DPX-400 100-MHz spectrometer in  $\text{CDCl}_3$  or  $\text{DMSO-}d_6$ . All signals are reported in ppm with the internal chloroform signal at 77.0 ppm or the internal DMSO signal at 39.5 ppm as standard. IR spectra were recorded on a JASCO FT-IR B4100 spectrophotometer with an ATR PRO410-S and a ZnSe prism. High-resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MicroMass (ESI) Q-TOF Ultima API.

### 1-Hydroxy-1λ<sup>3</sup>,2-benziodoxol-3(1H)-one (1)

Caution: This reaction should be carried out behind a safety shield! In accordance with a reported procedure,<sup>11</sup> NaIO<sub>4</sub> (77.2 g, 0.361 mol, 1.0 equiv) and 2-iodobenzoic acid (6; 89.5 g, 0.361 mmol, 1.0 equiv) were suspended in 30 vol% aq AcOH (700 mL) under air in a four-necked sulfonation flask equipped with a mechanical stirrer, a thermometer, and a condenser. The mixture was vigorously stirred and refluxed for 4 h then diluted with cold H<sub>2</sub>O (500 mL) and allowed to cool to r.t. in darkness. After 45 min, the suspension was added to H<sub>2</sub>O (1.5 L) and the crude product was collected by filtration, washed with ice-water (3  $\times$  300 mL) and cold acetone (3  $\times$  300 mL), and then air-dried in darkness overnight to give a colorless solid; yield: 77.3 g (0.292 mol, 81%).

IR (neat): 3083 (w), 3060 (w), 2867 (w), 2402 (w), 1601 (m), 1585 (m), 1564 (m), 1440 (m), 1338 (s), 1302 (m), 1148 (m), 1018 (w), 834 (m), 798 (w), 740 (s), 694 (s), 674 (m), 649 (m) cm<sup>-1</sup>.<sup>11</sup>

<sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ ):  $\delta = 8.02$  (dd, J = 7.7, 1.4 Hz, 1 H, ArH), 7.97 (m, 1 H, ArH), 7.85 (dd, J = 8.2, 0.7 Hz, 1 H, ArH), 7.71 (td, J = 7.6, 1.2 Hz, 1 H, ArH).

<sup>13</sup>C NMR (100 MHz, DMSO- $d_6$ ):  $\delta = 167.7, 134.5, 131.5, 131.1,$ 130.4, 126.3, 120.4.

**Trimethylsilyl(triisopropylsilyl)ethyne (8)** In a modification of a reported procedure, <sup>12</sup> HC=CTMS (7; 30.3 ml, 213 mmol, 1 equiv) was placed in a four-necked 500-mL flask equipped with a thermometer, a dropping funnel, an magnetic stirrer, and a N2 inlet. THF (330 mL) was added from a dropping funnel and the mixture was cooled to -78 °C. BuLi (86 mL, 0.21 mmol, 0.98 equiv) was added and the mixture was stirred for 5 min at -78 °C then warmed to 0 °C and stirred for 5 min. The mixture was then cooled again to -78 °C and TIPSCI (45.5 mL, 213 mmol, 1 equiv) was added dropwise from a dropping funnel. The mixture was allowed to warm to r.t. and stirred overnight. Sat. aq NH<sub>4</sub>Cl (300 mL) was added and the mixture was extracted with  $Et_2O$  (2 × 300 mL). The organic layer was dried (MgSO<sub>4</sub>), filtered, and concentrated. Distillation of the crude product (55 °C, 1.4 mbar) gave a colorless liquid; yield: 51.4 g (203 mmol, 95%).

IR (neat): 2959 (m), 2944 (m), 2896 (w), 2867 (m), 1464 (w), 1385 (w), 1250 (m), 996 (w), 842 (s), 764 (s), 675 (m), 660 (m) cm<sup>-1</sup>.<sup>12</sup>

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.08 (m, 21 H, TIPS), 0.18 (s, 9 H, TMS).

#### 1-[(Triisopropylsilyl)ethynyl]- $1\lambda^3$ ,2-benziodoxol-3(1*H*)-one (2; TIPS-EBX)

#### Caution: This reaction should be carried out behind a safety shield!<sup>13</sup>

In a modification of a reported procedure,<sup>10</sup> 2-iodosylbenzoic acid (1) (26.4 g, 100 mmol, 1.0 equiv) was placed in a four-necked flatbottomed flask equipped with a thermometer, a dropping funnel, a mechanical stirrer, and a  $N_2$  inlet. The system was flushed with  $N_2$ in three vacuum/N2 cycles before anhyd MeCN (350 mL) was added from a cannula. The white suspension was cooled to 4 °C and TMSOTf (20.0 mL, 110 mol, 1.1 equiv) was added dropwise over 15 min from a dropping funnel that was finally rinsed with anhyd MeCN (10 mL); no increase in temperature was observed. The ice bath was removed and the mixture was stirred for 15 min. TMSC=CTIPS (8; 28.0 g, 110 mmol, 1.1 equiv) was added dropwise from a dropping funnel over 15 min and the colorless suspension changed to a yellow soln. The dropping funnel was rinsed with anhyd MeCN (10 mL) and the mixture was stirred for 30 min. Pyridine (9.9 mL, 25 mmol, 1.1 equiv) was then added dropwise from a dropping funnel over 5 min. After 15 min, the mixture was transferred to a one-necked 1-L flask and concentrated to a solid under reduced pressure. The solid was dissolved in CH2Cl2 (250 mL) and transferred to a 2-L separatory funnel. The organic layer was removed and washed with 1 M aq HCl (150 mL). The aqueous layer was extracted with CH2Cl2 (250 mL) and the combined organic layers were washed with sat. aq NaHCO<sub>3</sub> ( $2 \times 250$  mL), dried (MgSO<sub>4</sub>), filtered, and concentrated under reduced pressure. The resulting solid (44.8 g) was recrystallized from MeCN (110 mL). The colorless solid that formed on cooling was filtered off, washed with hexanes (2  $\times$  40 mL), and dried for 1 h at 40 °C at 5 mbar to give white crystals; yield: 36.2 g (84.5 mmol, 85%); mp 173-177 °C (dec).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta = 8.37$  (m, 1 H, ArH), 8.28 (m, 1 H, ArH), 7.72 (m, 2 H, ArH), 1.13 (m, 21 H, TIPS).

 $^{13}$ C NMR (101 MHz, CDCl<sub>3</sub>):  $\delta = 166.4, 134.5, 132.3, 131.4, 131.4,$ 126.1, 115.6, 113.9, 64.7, 18.4, 11.1.<sup>10</sup>

#### 3-[(Triisopropylsilyl)ethynyl]-1H-indole (10)

TIPS-EBX (2; 5.14 g, 12.0 mmol, 1.2 equiv) was added to a stirred solution of AuCl (23 mg, 0.10 mmol, 0.01 equiv) and indole (9; 1.17 g, 10.0 mmol, 1.0 equiv) in  $Et_2O^{14}$  (200 mL) under air in a 500-mL flask. The flask was sealed and the mixture was stirred at r.t. for 36 h. Additional Et<sub>2</sub>O (250 mL) was added and the organic layer was washed twice with 0.1 M aq NaOH (250 mL). The aqueous layers were combined and extracted with Et<sub>2</sub>O (250 mL). The organic layers were combined, washed successively with sat. aq NaHCO<sub>3</sub> (250 mL) and brine (250 mL), dried (MgSO<sub>4</sub>), and concentrated under reduced pressure. The residue was purified by flash chromatography [PE-Et<sub>2</sub>O (8:2)] to give a brown solid: yield: 2.43 g (8.17 mol, 82%); mp 55–58 °C;  $R_f = 0.4$  (PE–Et<sub>2</sub>O, 7:3).

IR (neat): 3407 (m), 3062 (w), 2942 (s), 2891 (m), 2864 (s), 2152 (s), 1620 (w), 1532 (w), 1457 (s), 1416 (m), 1383 (w), 1341 (w), 1325 (m), 1239 (s), 1128 (m), 1071 (m), 996 (m), 910 (m), 883 (s), 774 (s), 742 (s), 676 (s), 658 (s), 628 (s) cm<sup>-1</sup>.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta = 8.11$  (br s, 1 H, NH), 7.79 (m, 1 H, ArH), 7.40 (d, J = 2.7 Hz, 1 H, ArH), 7.36 (m, 1 H, ArH), 7.26 (m, 2 H, ArH), 1.22 (m, 21 H, TIPS).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta = 135.1, 128.9, 128.3, 123.1, 120.8,$ 120.1, 111.4, 100.4, 99.3, 92.19, 18.8, 11.5.

HRMS (ESI): m/z [M + H]<sup>+</sup> calcd for C<sub>19</sub>H<sub>28</sub>NSi: 298.1991; found: 298.2001.

2-Iodobenzoic acid (6) was recovered by adjusting the pH of the aq NaOH fraction to 1 with concd. aq HCl and extracting the mixture with EtOAc ( $2 \times 300$  mL). The organic layers were combined, dried (MgSO<sub>4</sub>), and concentrated under reduced pressure to give 2-iodobenzoic acid (6) as a colorless solid; recovery: 2.18 g (8.79 mmol, 73% recovered).

# [(5-Hexyl-2-thienyl)ethynyl](triisopropyl)silane (9)

2-Hexylthiophene (11; 1.80 mL, 10.0 mmol, 1 equiv) was added to a stirred soln of AuCl (23 mg, 0.10 mmol, 0.01 equiv) in MeCN<sup>14</sup> (50 mL) under air in a 100-mL flask. After 2 min, TFA (0.891 mL, 12.0 mmol, 1.2 equiv) and TIPS-EBX (2; 5.14 g, 12.0 mmol, 1.2 equiv) were added. The flask was sealed and the mixture was stirred at r.t. for 4 d. Et<sub>2</sub>O (250 mL) was added and the organic layer was washed with 0.1 M aq NaOH ( $2 \times 300$  mL). The aqueous layers were combined and extracted with Et<sub>2</sub>O (250 mL). The organic layers were combined, washed successively with sat. aq NaHCO<sub>3</sub> (250 mL) and brine (250 mL) then dried (MgSO<sub>4</sub>) and concentrated under reduced pressure. The resulting oil was purified by flash chromatography (pentane) and the remaining starting material was removed by heating the oil at 70 °C and 0.5 mbar for 4 h to give a slightly yellow oil; yield: 2.83 g (8.11 mmol, 81%);  $R_f = 0.6$  (pentane).

IR (neat): 2958 (s), 2928 (s), 2865 (s), 2143 (s), 1535 (w), 1463 (s), 1382 (w), 1367 (w), 1243 (w), 1167 (m), 1074 (w), 1018 (m), 997 (m), 920 (w), 883 (s), 800 (s), 757 (s), 736 (s), 678 (s), 658 (s), 633 (s)  $cm^{-1}$ .

<sup>1</sup>H NMR:  $\delta$  = 7.08 (d, J = 3.5 Hz, 1 H, ArH), 6.65 (d, J = 3.5 Hz, 1 H, ArH), 2.80 (t, J = 7.5 Hz, 2 H, CH<sub>2</sub>), 1.68 (m, 2 H, CH<sub>2</sub>), 1.441.30 (m, 6 H, CH<sub>2</sub>), 1.15 (m, 21 H, TIPS), 0.93 (t, *J* = 6.1 Hz, 3 H, CH<sub>3</sub>).

<sup>13</sup>C NMR:  $\delta$  = 148.1, 132.4, 123.9, 121.0, 99.8, 94.3, 31.7, 31.6, 30.2, 28.7, 22.6, 18.7, 14.1, 11.4.

HRMS (ESI): m/z [M + H]<sup>+</sup> calcd for C<sub>21</sub>H<sub>37</sub>SSi: 349.2385; found: 349.2381.

2-Iodobenzoic acid (6) was recovered by adjusting the pH of the NaOH fraction to 2 with 1 M HCl and extracting the mixture with EtOAc ( $2 \times 250$  mL). The organic layers were combined, dried (MgSO<sub>4</sub>), and concentrated under reduced pressure to give 2-iodobenzoic acid (6) as a gray solid; recovery: 2.91 g (11.7 mmol, 97%).

#### N,N-Dibenzyl-4-[(triisopropylsilyl)ethynyl]aniline (14)

AuCl (59 mg, 0.025 mmol, 0.05 equiv) was added to a stirred soln of PhNBn<sub>2</sub> (**13**; 1.36 g, 5.00 mmol, 1 equiv) and TIPS-EBX (**2**; 3.00 g, 7.00 mmol, 1.4 equiv) in *i*-PrOH<sup>14</sup> (100 mL) under air in a 250mL flask and the mixture was stirred at r.t. for 24 h. EtOAc (200 mL) was added and the mixture was washed successively with 0.1 M aq NaOH (200 mL), sat. aq NaHCO<sub>3</sub> (200 mL), and brine (200 mL) then dried (MgSO<sub>4</sub>) and concentrated in vacuo. The resulting oil was purified by column chromatography [pentane–CH<sub>2</sub>Cl<sub>2</sub>(95:5 to 9:1)] to give **14** as a colorless oil [yield: 1.66 g (3.66 mmol, 73%)] together with a mixture of **14** and **13** [yield: 314 mg, (42 wt% **14** + 58 wt% **13**), equivalent to 6% product **14** + 13% recovered starting material **13**] as a colorless oil; total yield = 79%; yield based on recovered starting material: 91%;  $R_f$  (pentane–CH<sub>2</sub>Cl<sub>2</sub>, 9:1) = 0.15.

IR (neat): 3051 (w), 2943 (w), 2865 (w), 2143 (w), 1606 (m), 1516 (m), 1495 (w), 1454 (w), 1398 (w), 1360 (w), 1266 (m), 1241 (w), 1188 (w), 1075 (w), 997 (w), 955 (w), 884 (w), 841 (w), 818 (w), 737 (s), 698 (m), 677 (m) cm<sup>-1</sup>.

<sup>1</sup>H NMR (400 MHz,  $C_6D_6$ ):  $\delta$  = 7.37 (m, 2 H, ArH), 7.18–7.01 (m, 6 H, ArH), 6.95 (m, 4 H, ArH), 6.42 (m, 2 H, ArH), 4.15 (s, 4 H, CH<sub>2</sub>), 1.21 (m, 21 H, TIPS).

<sup>13</sup>C NMR (101 MHz,  $C_6D_6$ ):  $\delta = 149.3$ , 138.4, 133.9, 128.9, 127.3, 126.9, 112.4, 111.8, 109.6, 87.6, 53.9, 19.1, 11.9.

HRMS (ESI):  $m/z [M + H]^+$  calcd for  $C_{31}H_{40}NSi^+$ : 454.2925; found: 454.2913.

2-Iodobenzoic acid (6) was recovered by adjusting the pH of the NaOH fraction to 2 with 1 M aq HCl and extracting with EtOAc  $(2 \times 250 \text{ mL})$ . The organic layers were combined, dried (MgSO<sub>4</sub>), and concentrated under reduced pressure to give 2-iodobenzoic acid (6) as a gray solid: recovery: 1.25 g (5.03 mmol, 72%).

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# References

- (1) Zhdankin, V. V.; Stang, P. J. Chem. Rev. 2008, 108, 5299.
- (2) (a) Eisenberger, P.; Gischig, S.; Togni, A. Chem. Eur. J.
  2006, 12, 2579. (b) Kieltsch, I.; Eisenberger, P.; Togni, A. Angew. Chem. Int. Ed. 2007, 46, 754. (c) Wiehn, M. S.; Vinogradova, E. V.; Togni, A. J. Fluorine Chem. 2010, 131, 951.
- (3) (a) Brand, J. P.; Fernández González, D.; Nicolai, S.; Waser, J. *Chem. Commun. (Cambridge)* 2011, 47, 102. (b) Reagents 2, 3 and 4 are now also commercially available.
- (4) For a review, see: Zhdankin, V. V.; Stang, P. J. *Tetrahedron* **1998**, *54*, 10927.
- (5) Fernández González, D.; Brand, J. P.; Waser, J. Chem. Eur. J. 2010, 16, 9457.
- (6) (a) Nicolai, S.; Erard, S.; Fernández González, D.; Waser, J. *Org. Lett.* 2010, *12*, 384. (b) Nicolai, S.; Piemontesi, C.; Waser, J. *Angew. Chem. Int. Ed.* 2011, *50*, 4680.
- (7) For reviews on direct alkynylation, see: (a) Dudnik, A. S.; Gevorgyan, V. *Angew. Chem. Int. Ed.* **2010**, *49*, 2096.
  (b) Messaoudi, S.; Brion, J. D.; Alami, M. *Eur. J. Org. Chem.* **2010**, 6495.
- (8) (a) Brand, J. P.; Charpentier, J.; Waser, J. Angew. Chem. Int. Ed 2009, 48, 9346. (b) Brand, J. P.; Chevalley, C.; Waser, J. Beilstein J. Org. Chem. 2011, 7, 565. (c) Brand, J. P.; Waser, J. Angew. Chem. Int. Ed. 2010, 49, 7304. (d) Brand, J. P.; Waser, J. Org. Lett. 2012, 14, 744.
- (9) (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron* Lett. 1975, 16, 4467. (b) Chinchilla, R.; Najera, C. Chem. Rev. 2007, 107, 874.
- (10) Zhdankin, V. V.; Kuehl, C. J.; Krasutsky, A. P.; Bolz, J. T.; Simonsen, A. J. J. Org. Chem. **1996**, 61, 6547.
- (11) Kraszkiewicz, L.; Skulski, L. ARKIVOC 2003, (iv), 120.
- (12) Helal, C. J.; Magriotis, P. A.; Corey, E. J. J. Am. Chem. Soc. 1996, 118, 10938.
- (13) Differential scanning calorimetry showed that TIPS-EBX undergoes exothermic degradation at 187 °C.
- (14) The commercial solvent was used without additional drying or purification.